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55331 (US). SAWCHUK, Ronald, J. [US/US]; 1702  
- 20th Avenue N.W., New Brighton, MN 55112 (US).  
FURCHT, Leo, T. [US/US]; 2100 West 21st Street,  
Minneapolis, MN 55405 (US).

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(74) Agent: MUETING, Ann, M.; Mueting, Raasch & Geb-  
hardt, P.A., P.O. Box 581415, Minneapolis, MN 55458-  
1415 (US).

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(71) Applicants (*for all designated States except US*): RE-  
GENTS OF THE UNIVERSITY OF MINNESOTA  
[US/US]; Suite 600 Gateway, 200 Oak Street SE, Min-  
neapolis, MN 55455 (US). BOARD OF REGENTS,  
THE UNIVERSITY OF TEXAS SYSTEM [US/US];  
201 West 7th Street, Austin, TX 78701 (US). SENTRON  
MEDICAL, INC. [US/US]; Suite 600, 4445 Lake Forest  
Drive, Cincinnati, OH 45242 (US).

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(72) Inventors; and

(75) Inventors/Applicants (*for US only*): MCCARTHY,  
James, B. [US/US]; 2555 - 37th Avenue South, Min-  
neapolis, MN 55406 (US). MILESKEI, William, J.  
[US/US]; 4220 Pirates Beach, Galveston, TX 77554 (US).  
JAMIESON, Gordon, A., Jr. [US/US]; 3422 Ault View  
Avenue, Cincinnati, OH 45208 (US). LOW, Walter, C.  
[US/US]; 19845 Sweetwater Curve, Shorewood, MN

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ning of each regular issue of the PCT Gazette.*

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(54) Title: METHODS OF USE OF BETA 1-INTEGRIN INHIBITORS

(57) Abstract: The present invention provides methods that use agents capable of one or more of the following: inhibiting leukocyte mediated destruction of tissues, especially after injuries to tissue due to heat or cold (i.e., burns or frostbite), light, electricity, chemicals, or other agents that cause tissue injury and destruction; inhibiting leukocyte mediated destruction of tissues after myocardial infarction, CNS ischemic injury (e.g., stroke), angioplasty, surgical incisions, injury-mediated trauma, and transplant reperfusion; inhibiting angiogenesis; inhibiting cancer cell metastasis, motility, and/or migration within tissue; restoring and/or potentiating the induction of programmed cell death in cancerous tissues or restoring normal cellular phenotype to cancerous tissue; inhibiting osteoclast adhesion and bone resorption; and/or inhibiting stem cell adhesion to bone marrow.

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/07680

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K38/06 A61K38/08 A61K38/07 A61P19/00 A61P17/00  
A61P41/00 A61P9/00 A61P35/00 A61P25/00 A61P29/00  
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## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EPO-Internal, MEDLINE, PAJ, WPI Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 840 691 A (EVERETT JEFFREY E ET AL) 24 November 1998 (1998-11-24) abstract column 2, line 2 - line 22 column 2, line 30 column 2, line 48 - line 51 column 3, paragraph 49 - paragraph 50 column 9, line 9 - column 10, line 6 claims 1,4-6 --- -/--	1,4,5,7, 8,32,38

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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\*&\* document member of the same patent family

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European Patent Office, P.B. 5818 Patentaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040. Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>YANAKA KIIYOYUKI ET AL: "Neuronal protection from cerebral ischemia by synthetic fibronectin peptides to leukocyte adhesion molecules." JOURNAL OF CEREBRAL BLOOD FLOW AND METABOLISM, vol. 16, no. 6, 1996, pages 1120-1125, XP000952738 ISSN: 0271-678X cited in the application abstract page 1121, column 1, line 13 - line 26 page 1121, column 2, line 48 - line 49 page 1122, column 1, line 3 - line 6 page 1123, column 1, paragraph 2 - paragraph 3 page 1123, column 2, line 1 - line 6 page 1124, column 1, last paragraph -column 2, paragraph 1</p>	1,4,5,38
X	<p>HINES KEITH L ET AL: "Synthetic fibronectin peptides interrupt inflammatory cell infiltration in transforming growth factor beta-1 knockout mice." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES, vol. 91, no. 11, 1994, pages 5187-5191, XP002150881 1994 ISSN: 0027-8424 cited in the application abstract page 5187, column 2, paragraph 3 page 5188, column 1, paragraph 3 page 5189, column 1, last paragraph -page 5190, column 2, paragraph 1 page 5191, column 1, last paragraph</p>	1,4,5,7,38
X	<p>MOHRI HIROSHI: "Interaction of fibronectin with integrin receptors: Evidence by use of synthetic peptides." PEPTIDES (TARRYTOWN), vol. 18, no. 6, 1997, pages 899-907, XP000952794 ISSN: 0196-9781 page 900, column 2, last paragraph -page 901, column 1, paragraph 3 page 901, column 1, paragraph 6 -column 2, paragraph 1</p> <p style="text-align: center;">--- -/--</p>	25

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/07680

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>LEVREY H ET AL: "Induction of fibroblast apoptosis by soluble fibronectin peptides."</p> <p>MOLECULAR BIOLOGY OF THE CELL, vol. 8, no. SUPPL., November 1997 (1997-11), page 181A</p> <p>XP000952737</p> <p>37th Annual Meeting of the American Society for Cell Biology; Washington, D.C., USA; December 13-17, 1997</p> <p>ISSN: 1059-1524</p> <p>abstract</p>	28-30
A	<p>HUEBSCH JOSEPH C ET AL: "Endothelial cell interactions with synthetic peptides from the carboxyl-terminal heparin-binding domains of fibronectin."</p> <p>CIRCULATION RESEARCH, vol. 77, no. 1, 1995, pages 43-53,</p> <p>XP000952796</p> <p>ISSN: 0009-7330</p> <p>abstract</p> <p>page 44, column 2, paragraph 1 - paragraph 2; table 1</p> <p>page 47, last paragraph -page 48, paragraph 2</p> <p>page 52, paragraph 2</p>	25
A	<p>WO 89 01942 A (UNIV MINNESOTA)</p> <p>9 March 1989 (1989-03-09)</p> <p>abstract</p> <p>page 9, line 3 - line 19</p> <p>table 3</p>	
A	<p>PROSPER FELIPE ET AL: "Mobilization and homing of peripheral blood progenitors is related to reversible downregulation of alpha4beta1 integrin expression and function."</p> <p>JOURNAL OF CLINICAL INVESTIGATION, vol. 101, no. 11, 1 June 1998 (1998-06-01), pages 2456-2467,</p> <p>XP002150882</p> <p>ISSN: 0021-9738</p> <p>the whole document</p>	35

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# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/07680

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	<p>CHAPPELL VICKY L ET AL: "Inhibition of leukocyte-mediated tissue destruction by synthetic fibronectin peptide (Trp-9-Tyr)."</p> <p>JOURNAL OF BURN CARE &amp; REHABILITATION, vol. 20, no. 6, November 1999 (1999-11), pages 505-510, XP000952744</p> <p>ISSN: 0273-8481</p> <p>abstract</p> <p>page 505, column 2, last paragraph -page 506, column 1, paragraph 2</p> <p>page 506, column 1, line 37 - line 47</p> <p>page 509, paragraph 2</p>	1-4,6, 13-20
P,A	<p>WO 99 37669 A (BRIENZO ANGELA ;FURCHT LEO T (US); UNIV MINNESOTA (US); MCCARTHY J)</p> <p>29 July 1999 (1999-07-29)</p> <p>cited in the application</p> <p>abstract</p> <p>page 2, line 1 - line 18</p> <p>page 5, line 5 - line 7</p> <p>page 6, line 11 - line 18</p> <p>page 6, line 27 - line 9</p> <p>page 9, line 3 - line 5</p>	

# INTERNATIONAL SEARCH REPORT

Information on patent family members

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 5840691	A	24-11-1998	US 5591719 A	07-01-1997
			EP 0673384 A	27-09-1995
			WO 9413692 A	23-06-1994
			SG 49017 A	18-05-1998
WO 8901942	A	09-03-1989	US 4839464 A	13-06-1989
			US 5019646 A	28-05-1991
			AT 87936 T	15-04-1993
			AU 605637 B	17-01-1991
			AU 2385988 A	31-03-1989
			CA 1305084 A	14-07-1992
			DE 3880139 D	13-05-1993
			DE 3880139 T	21-10-1993
			EP 0366728 A	09-05-1990
			JP 2690767 B	17-12-1997
			JP 3500046 T	10-01-1991
			US 5116368 A	26-05-1992
			US 5171271 A	15-12-1992
			US 5147797 A	15-09-1992
			US 5294551 A	15-03-1994
			ZA 8806314 A	26-04-1989
WO 9937669	A	29-07-1999	NONE	